

REMARKS

In the Office Action dated October 29, 2003, claims 1-56 were examined with the result that all claims were rejected. In response, Applicant submits the following comments. In view of these comments, reconsideration of this application is requested.

In the Office Action, the obviousness rejections of claims 1-56 under 35 USC §103(a) over DeLuca et al '410 and/or DeLuca et al '928 were withdrawn. The only remaining rejections made by the Examiner are under the doctrine of obviousness type double patenting. The Examiner alleges that claims 1-56 are unpatentable over DeLuca et al '410 and/or DeLuca et al '928 under the doctrine of obviousness type double patenting. Although the Examiner acknowledges Applicant's showing that the presently claimed compounds have unexpected properties when compared to the closest exemplified prior art compounds, the Examiner nevertheless maintains the obviousness type double patenting rejection in view of the '410 and '928 references. The Examiner states that the issue under the doctrine of obviousness type double patenting is whether the claimed invention is made obvious in view of the cited references. The basis for the Examiner's conclusion is that the genus of compounds in the two references encompass the presently claimed compounds, and further that each of these references contain specific teachings relating to (a) either 2-alkyl or 2-alkylidene derivatives having radicals of 1-10 carbon atoms and (b) either "ethyl" or "ethylene" as the substituent in the 2-position of compounds named in either the '410 or the '928 references. In response, Applicant has the following comments.

It is well established that one person may obtain a valid patent on an improvement over what is generally claimed in a first patent even though the improvement (i.e. in this case a chemical species) might be dominated by the basic or general patent of another (i.e. in this case a chemical genus). The species must meet the customary standards of patentability, including the requirement that it not be obvious in light of the basic or general patent which claims the genus. However, the Federal Circuit Court of Appeals as

well as the U.S. PTO have followed the rule that the determining factor in deciding whether or not there is double patenting is the existence of a patentable difference between two sets of claims. In other words, the same inventor may obtain separate patents on the basic invention (the genus) and the improvement (the species) if, but only if, another inventor could have obtained the second patent on that improvement (species).

It is elementary that readability of a claim on the subject matter of another claim (domination) is neither determinative of the obviousness-type double patenting issue nor demonstrative that claims are directed to the same invention. For example, in the case of In re Kaplan, 789 F2d 1574, 229 USPQ 678 (Fed. Cir. 1986), the Federal Circuit held that a double patenting rejection cannot be justified solely on the ground that the subject matter of a claim in a second patent or patent application is "dominated" by the claims in a first patent.

"By domination we refer, in accordance with established patent law terminology, to that phenomenon, which grows out of the fact that patents have claims, whereunder one patent has a broad or 'generic' claim which 'reads on' an invention defined by a narrower or more specific claim in another patent, the former 'dominating' the latter because the more narrowly claimed invention cannot be practiced without infringing the broader claim.... In possibly simpler terms, one patent dominates another if a claim of the first patent reads on a device built or process practiced according to the second patent disclosure. This commonplace situation is not, per se, double patenting...."

The court in Kaplan stressed that to establish obviousness type double patenting there must be clear evidence other than mere domination to establish why the variation or improvement (the species) would have been obvious. The evidence utilized by the Examiner is that the genus of compounds disclosed in '410 and '928 encompass the presently claimed compounds, and there are specific teachings regarding "ethyl" as an

alkyl substituent in the 2-position in the '410 reference and "ethylene" as the alkylidene substituent in the 2-position in the '928 reference.

However, as discussed above in the Kaplan case, the mere fact that a reference discloses a genus of compounds which encompass the presently claimed compounds is insufficient to conclude that the species of compounds claimed in the present application would have been obvious. Therefore, one must look at whether the fact that a listing of possible 2-ethyl and 2-ethylene compounds would be motivation to one skilled in this art to select Applicant's presently claimed compounds.

A key issue in a finding of obviousness is a determination whether one of ordinary skill in the relevant art would have been motivated to make the claimed invention or whether there is some suggestion to make the claimed invention in light of the prior art teachings, i.e. to select the claimed species from the disclosed prior art genus. To address this key issue, various factors should be considered including (a) the size of the genus; (b) the express teachings of the prior art; (c) the teachings of structural similarity in the prior art; (d) the teachings of similar properties or uses in the prior art; and (e) the predictability of the technology.

With regard to the size of the genus, it is clear that the claimed genus in the '410 and '928 references is large. There are a high number of compounds covered by the 2-alkyl and 2-alkylidene structural formulae of the '410 and '928 references. In contrast, Applicant is claiming herein only four compounds covered by the genus of '410 and only four compounds covered by the genus of '928. Although there is no absolute correlation between the size of the prior art genus and a conclusion of obviousness, it is clear that the genus taught in the prior art references is not so small that it would anticipate the claimed species, i.e. the prior art '410 and '928 references do not disclose a small recognizable class of compounds all with common properties, but instead discloses a very large genus of compounds. This factor thus weighs in favor of unobviousness.

With regard to the express teachings in the '410 and '928 references, there is nothing in either of these two references which expressly suggests to one skilled in the art to select the herein claimed 2-ethyl and/or 2-ethylidene compounds. Although the Examiner points to a listing of compounds found at columns 5 and 6 of the '410 reference, it should be noted that none of the four compounds claimed herein are specifically listed in that listing of compounds. The closest compound listed would be a 2-ethyl-24-homo compound, but such compound has a different side chain than the instantly claimed compounds. The same is true of the listing of compounds found at columns 6 and 7 of the '928 reference. In addition, there is no express statement or teaching in either the '410 or '928 reference suggesting to one skilled in this art that the instantly claimed 2-ethyl or 2-ethylidene compounds should be selected for any particular reason from the large genus of compounds disclosed therein. In other words, there is no statement that such compounds are "preferred" or "desirable" over any of the remaining compounds covered by the genus which other wise might direct one skilled in this art to select the instantly claimed compounds out of the genus of compounds. Thus, there is no specific express teaching of the instantly claimed compounds in either of the two prior art references cited by the Examiner. This again weighs in favor of unobviousness.

With regard to teachings of structural similarity, those same listing of compounds found in the '410 and '928 patents state that they are "preferred examples" of the 2-alkyl and 2-alkylidene compounds disclosed and claimed in those two references. As noted above, the closest compounds that are structurally similar to those instantly claimed are the 2-ethyl- and/or 2-ethylene-24-homo compounds. The closest compounds disclosed in either '410 or '928 are the 2-methyl- and/or 2-methylene-19-nor-1,25-dihydroxyvitamin D₃ compounds. These compounds are structurally similar to those instantly claimed with the difference being Applicant herein claims 2-ethyl rather than 2-methyl compounds and/or 2-ethylidene rather than 2-methylene compounds. Based on the premise that structurally similar species usually have similar properties, one would normally conclude

that the instantly claimed species would be obvious in view of the compounds taught in '410 and/or '928. However, a key issue in this regard would be whether Applicant's claimed compounds yielded unexpected results that differ from those taught with respect to the broad generic claim of the '410 and '928 patents. In this regard, Applicant previously submitted a comparison of biological activities, and Applicant notes that the Examiner has agreed that the presently claimed compounds have different and unexpected properties in view of the fact that the Examiner has withdrawn the §103(a) obviousness rejections over '410 and '928. Once again, this factor weighs in favor of unobviousness.

With regard to the teachings of similar properties, Applicant has already noted that the properties taught in the '410 and '928 references with regard to the prior art genus are significantly different than the properties of the claimed species. Since it is the properties that provide real world motivation for a person of ordinary skill in the art to make species structurally similar to those in the prior art, evidence that the instantly claimed compounds have properties different from those taught in the '410 and '928 references weighs in favor of a conclusion that the instantly claimed compounds would not be obvious.

With regard to the teachings of similar uses, it is to be noted that the instantly claimed compounds have utility for the treatment of metabolic bone disease, psoriasis, cancer, imbalance in the immune system, arthritis, alopecia, various skin conditions, hypocalcemia, hypoparathyroidism and inflammatory bowel diseases. Same and/or similar pharmaceutical uses are taught for the genus of compounds in '410 and '928 references. Thus, this factor weighs in favor of a conclusion that the instantly claimed compounds would have been obvious. However, this factor alone cannot tip the scale in favor of obviousness, especially when the remaining factors discussed herein all weigh in favor of unobviousness.

With regard to the predictability of the technology, it is clear that the present technology is unpredictable. As stated in Calverley et al U.S. Patent 5,206,229 at column 3, lines 26-37:

"The fact that there are only small structural differences between the above compounds indicates that the present state of knowledge does not allow prediction of the structure of vitamin D analogues which will show a favorable degree of selectivity, as reflected by a higher cell differentiating activity in vitro compared to the binding affinity for intestinal vitamin D receptor in vitro. Furthermore, the matter is complicated by the observation that receptor binding affinities in vitro are not always paralleled by in vivo studies, probably reflecting a pharmacokinetic difference between the compounds."

If the technology is unpredictable, it is less likely that structurally similar species will render a claimed species obvious because it may not be reasonable to infer they would share similar properties. Under the present circumstances, Applicant has shown that it is not reasonable to infer that they would have similar properties because in fact they do not have similar properties.

In summary, Applicant believes that a weighing of the above evidence and arguments leads one to conclude that the instantly claimed species would not have been obvious in view of the genus taught is either the '410 reference or the '928 reference. There is clearly no explicit motivation or suggestion in either the '410 reference or the '928 reference to select the presently claimed four compounds from the large genus taught in these prior art references. Based on the evidence as a whole, Applicant believes that the claimed invention would not have been obvious to one of ordinary skill in the relevant art at the time the invention was made.

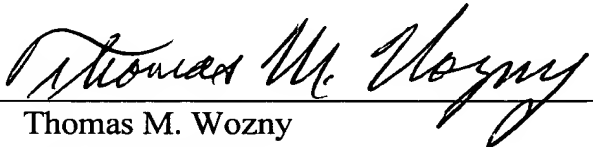
Accordingly, Applicant requests the Examiner withdraw the rejections based on obviousness-type double patenting.

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An effort has been made to place this application in condition for allowance and such action is earnestly requested.

Respectfully submitted,

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